

REMARKS

Claims 1-17 and 21-26 are pending. Applicants have amended claim 6 to correct minor typographical errors. Applicants have also amended claims 1 and 15, to better define the claimed invention. The amendment is supported in the specification at least in the Abstract, and at page 4, lines 18-34. Thus, the amendments do not contain new matter.

The Office has withdrawn the rejections under 35 U.S.C. § 112, second paragraph in view of canceled claims 18-20. The other rejections were maintained. Applicants address each rejection in more detail below.

Rejections under 35 U.S.C. § 102

A. Claims 1-5, 7-10 and 13 are novel under the Okihira reference

Claims 1-5, 7-10 and 13 remain rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Okihara *et al.* (J. Macromol. Sci. Phys. B30: 119-140 (1991)). In particular, the Office indicated that “[t]he components of the stereocomplex of Okihara are poly(L-lactide) and poly(D-lactide) and these are the oligomers or co-oligomers that are recited in the depended [sic] claims and thus they ought to be water-soluble.” (Office Action, page 3). Applicants must respectfully disagree, and address the rejection in view of the amended claims.

Claim 1 as amended relates to a hydrogel composition comprising a mixture of two water soluble or water dispersible polymers substituted with oligomers or co-oligomers at least partly formed from monomers of opposite chirality. For example, oligomerized monomers are grafted to a water soluble polymer such as dextran, starch, cellulose, albumin, lysozyme, poly(aminoacids), poly(lysine), poly(glutamic acid), polymethacrylates, polymethacrylamides, poly(vinylalcohol), poly(ethylene glycol), water soluble polyphosphazenes, or mixtures thereof. (See e.g., Abstract; specification at page 11, lines 2-10; and Figure 1). Example 6 in the specification also describes the preparation of L- and D-lactic acid oligomers coupled to a water soluble polymer such as dextran, and gelation of the dextran-lactate solutions.

The Okihara reference fails to anticipate for at least two reasons. First, Okihara is silent regarding water soluble or water dispersible polymers, let alone water soluble polymers substituted with oligomers or co-oligomers. Okihara describes a crystallized stereocomplex from an equimolar mixture of poly(L-lactide) (PLLA) and poly(D-lactide) (PDLA), the homopolymers of L-lactic acid and D-lactic acid respectively, which are crystalline polymers and mostly insoluble in water. (See e.g., van Nostrum *et al.*, ACS Symposium Series 2003, 846: 129-141; see page 5 of manuscript attached at Exhibit 1). Furthermore, none of the homopolymers described in Okihara to form the stereocomplex is grafted to a water soluble polymer.

Second, Okihara is silent regarding hydrogel compositions comprising a mixture of water soluble or water dispersible polymers in an aqueous system. Because the individual enantiomeric polymers taught in Okihara are mostly insoluble in water, stereocomplex crystals are formed from an organic solvent containing PLLA and PDLA in an equimolar fraction. Alternatively, stereocomplex crystals may be formed in the melt, such as by annealing films made from an equimolar mixture of PLLA and PDLA. (See, Okihara *et al.*, Experimental Section at pages 120-121).

Because the Okihara reference fails to describe hydrogel compositions comprising a mixture of water soluble or water dispersible polymers in an aqueous system, substituted with oligomers or co-oligomers at least partly formed from monomers of opposite chirality, the claims are not anticipated. Accordingly, Applicants respectfully request that this rejection be withdrawn.

B. Claims 1-10, 14 and 21-26 are novel under the Hennink reference

Claims 1-10, 14 and 21-2 [sic] also remain rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Hennink *et al.*, (WO 98/00170). Applicants must again respectfully disagree.

In particular, the Office alleged that the “instant claims do not exclude hydrolysable bonds consisting of two interpenetrating networks.” (Office Action, page 3). As the Office indicated, Hennink discloses a biodegradable hydrogel that contains hydrolysable bonds, where the

hydrogel consists of two interpenetrating polymer networks interconnecting to one another through hydrolysable spacers. (Office Action, page 3, emphasis added). By definition, hydrolysable spacers are covalently attached, with the bond capable of being split or altered by water. In contrast, pending claim 1 requires that the polymers from mixture (A) interact noncovalently with polymers from mixture (B). Thus, the claims exclude hydrolysable bonds consisting of two interpenetrating networks.

Furthermore, the Hennink reference fails to teach hydrogel compositions comprising water soluble polymers containing oligomers partly formed from monomers of opposite chirality. In Example 5, Hennink describes the preparation of hydrogels by a free radical polymerization of methacrylated dextran prepared according to Examples 1-4. In Example 3, Hennink describes the synthesis of dex-lactate-HEMA by coupling L-lactide and HEMA thereby forming HEMA-lactate, and coupling carbonyldiimidazole activated HEMA-lactate to dextran. Thus, Hennink only describes a water soluble polymer containing oligomers partly formed from one chiral monomer (*i.e.*, L-lactide).

Based on the above, the claims are not anticipated under Hennink. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 103

Claim 12 remain rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Hennink *et al.* The Office concedes that Hennink does not teach a degree of substitution of 3-25, but alleges that “[o]ne having ordinary skill in the art would have been motivated to prepare a stereocomplex hydrogel composition with a varying degree of substitution with the expectation of obtaining a hydrogel with the desired cross-linked network.” (Office Action, page 4). Moreover, the Office again alleged that “[t]he instant claims do not exclude hydrolysable bonds. . . .” *Id.* Applicants must again respectfully disagree.

As previously indicated, pending claim 1 requires that the polymer mixtures interact noncovalently. Because claim 11 depends from claim 1, claim 11 contains all the limitations in claim 1 and excludes hydrolysable bonds consisting of two interpenetrating networks. Because the Hennink reference neither teaches nor suggests hydrogels containing polymers mixtures that interact noncovalently, claim 11 is nonobvious under Hennink. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Furthermore, claim 12 remain rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Okihara *et al.* The Office concedes that Okihara is silent on the length of monomers, but that “[o]ne having ordinary skill in the art would have been motivated to take a mixture of lactides having the appropriate lengths with the expectation that a stereocomplex hydrogel will form.” (Office Action, page 5). The Office also alleged that the “composition of Okihara are inherently hydrogels because the monomers or oligomers of Okihara are the same as those recited in the dependent claims.” *Id.* Applicants must again respectfully disagree.

Because claim 12 depends from claim 1, claim 12 contains all the limitations in claim 1. As previously indicated, Okihara only teaches a stereocomplex of PLLA and PDLA, homopolymers which are mostly insoluble in water. Because Okihara neither suggests nor describes hydrogel compositions comprising a mixture of water soluble or water dispersible polymers in an aqueous system, substituted with oligomers or co-oligomers at least partly formed from monomers of opposite chirality, claim 12 is nonobvious under Okihara. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Further, claims 15-17 remain rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over De Jong *et al.* (Macromolecules 31: 6397-6402 (1998), in view of Brannon-Peppas (Int. J. Pharm. 116: 1-9 (1995)). The Office alleged that “[o]ne having ordinary skill in the art would have been motivated to include active agents in the lactide hydrogel formulation of De Jong with the expectation that the stereocomplex lactide hydrogel would serve as a carrier.” (Office Action, page 10). Applicants must again respectfully disagree, and address the rejection in view of the amended claims.

Claim 15 as amended relates to a process for preparing a hydrogel comprising mixing two mixtures of a water soluble or water dispersible polymer substituted with the product from polymerizing a monomer of opposite chirality. For example, hydrogels are prepared from gelation of L- and D-lactic acid oligomers coupled to a water soluble polymer such as dextran. (See, Example 6).

De Jong is silent regarding water soluble or water dispersible polymers, let alone water soluble polymers substituted with oligomers or co-oligomers. As the Office indicated, De Jong describes stereocomplex formation in blends of homo- or copolymers of D- and L-lactides, or in blends of random copolymers (See e.g., de Jong, page 6397, emphasis added). However, none of the homo- or copolymers is incorporated within a water soluble or water dispersible polymer. Because De Jong neither teaches nor suggests hydrogel preparation from mixing homo- or copolymers incorporated within a water soluble or water dispersible polymer, claims 15-17 are non-obvious under De Jong.

Furthermore, De Jong's failure to teach the process described in pending claims 15-17 is not remedied by Brannon-Pappas, as Brannon-Pappas is also silent regarding hydrogels and water soluble or water dispersible polymers. Brannon-Pappas merely describes the use of biodegradable polymers in controlled drug delivery. Thus, even if De Jong and Brannon-Pappas were combined, the combination fails to teach a process for preparing hydrogels by mixing two mixtures of a water soluble or water dispersible polymer substituted with the product from polymerizing a monomer of opposite chirality.

Based on the above, claims 15-17 are nonobvious under De Jong, in view of Brannon-Pappas. Thus, Applicants respectfully request that this rejection be withdrawn.

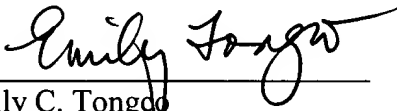
In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is

determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 313632001000. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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